1: Nature 1999 Feb 18;397(6720):579-83 Related Articles, Links

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Related Resources

Comment in:

- Nature. 1999 Feb 18;397(6720):568-9.

nature

A mammalian protein with specific demethylase activity for mCpG DNA.

Bhattacharya SK, Ramchandani S, Cervoni N, Szyf M.

Department of Pharmacology and Therapeutics, McGill University, Montreal, QC, Canada.

DNA-methylation patterns are important for regulating genome functions, and are determined by the enzymatic processes of methylation and demethylation. The demethylating enzyme has now been identified: a mammalian complementary DNA encodes a methyl-CpG-binding domain, bears a demethylase activity that transforms methylated cytosine bases to cytosine, and demethylates a plasmid when the cDNA is translated or transiently transfected into human embryonal kidney cells in vitro. The discovery of this DNA demethylase should provide a basis for the molecular and developmental analysis of the role of DNA methylation and demethylation.

PMID: 10050851 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

FILE 'HOME' ENTERED AT 16:55:01 ON 15 MAY 2003)

FILE 'CAPLUS' ENTERED AT 16:55:38 ON 15 MAY 2003

L1	0	S	DNA DEMETHYLASE (A) INHIBITOR
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L3	0	S	L2 (A) INHIBITION
L4	0	S	IMIDAZOLE (A) DNA DEMETHYLASE

2 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1999:218801 CAPLUS
DN 131:29241
TI **DNA demethylase** is a processive enzyme
AU Cervoni, Nadia; Bhattacharya, Sanjoy; Szyf, Moshe
CS Department of Pharmacology, McGill University, Montreal, QC, H3G 1Y6, Can.
SO Journal of Biological Chemistry (1999), 274(13), 8363-8366
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 7-4 (Enzymes)
AB DNA methylation patterns are generated during development by a sequence of methylation and demethylation events. We have recently demonstrated that mammals bear a bona fide demethylase enzyme that removes Me groups from methylated cytosines. A general genome wide demethylation occurs early in development and in differentiating cell lines. This manuscript tests the hypothesis that the demethylase enzyme is a processive enzyme. Using bisulfite mapping, this report demonstrates that demethylase is a processive enzyme and that the rate-limiting step in demethylation is the initiation of demethylation. Initiation of demethylation is detd. by the properties of the sequence. Once initiated, demethylation progresses processively. We suggest that these data provide a mol. explanation for global hypomethylation.
ST **DNA demethylase** hypomethylation

NCBI Entrez Protein

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

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Entrez Protein

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Items 1-20 of 42 Page 1 of 3 Next

☐1: NP_004167 BLink, Domains, Links
sterol regulatory element binding transcription factor 1; sterol regulatory element binding protein-1 [Homo sapiens]
gi|22547195|ref|NP_004167.3|[22547195]

☐2: XP_016472 BLink, Links
similar to Cytochrome P450 51A1 (CYPL1) (P450L1) (Sterol 14-alpha demethylase) (Lanosterol 14-alpha demethylase) (LDM) (P450-14DM) [Homo sapiens]
gi|13650621|ref|XP_016472.1|[13650621]

☐3: NP_056647 BLink, Domains, Links
methyl-CpG binding domain protein 2 testis-specific isoform [Homo sapiens]
gi|7710145|ref|NP_056647.1|[7710145]

Related resources

☐4: NP_003917 BLink, Domains, Links
methyl-CpG binding domain protein 3 [Homo sapiens]
gi|4505119|ref|NP_003917.1|[4505119]

☐5: NP_003918 BLink, Domains, Links
methyl-CpG binding domain protein 2 isoform 1 [Homo sapiens]
gi|4505117|ref|NP_003918.1|[4505117]

☐6: P10614 BLink, Domains, Links
Cytochrome P450 51 (CYPL1) (P450-L1A1) (Sterol 14-alpha demethylase) (Lanosterol 14-alpha demethylase) (P450-14DM)
gi|117176|sp|P10614|CP51_YEAST[117176]

☐7: P14263 BLink, Domains, Links
Cytochrome P450 51 (CYPL1) (P450-L1A1) (Sterol 14-alpha demethylase) (Lanosterol 14-alpha demethylase) (P450-14DM)
gi|117175|sp|P14263|CP51_CANTR[117175]

☐8: BAC65961 BLink, Domains, Links
putative cytochrome P450(Obtusifoliol 14-alpha demethylase) [Oryza sativa (japonica cultivar-group)]
gi|29027845|dbj|BAC65961.1|[29027845]

☐**9:** NP_056723 BLink, Domains, Links
methyl-CpG binding domain protein 1 isoform PCM1 [Homo sapiens]
gi|21464119|ref|NP_056723.2|[21464119]

☐**10:** NP_056671 BLink, Domains, Links
methyl-CpG binding domain protein 1 isoform 1 [Homo sapiens]
gi|21464117|ref|NP_056671.2|[21464117]

☐**11:** NP_056670 BLink, Domains, Links
methyl-CpG binding domain protein 1 isoform 2 [Homo sapiens]
gi|21464115|ref|NP_056670.2|[21464115]

☐**12:** NP_604391 BLink, Domains, Links
cAMP responsive element binding protein 1 isoform B; cAMP-response element-binding protein-1; active transcription factor CREB; transactivator protein [Homo sapiens]
gi|19745184|ref|NP_604391.1|[19745184]

☐**13:** NP_002375 BLink, Domains, Links
methyl-CpG binding domain protein 1 isoform 4 [Homo sapiens]
gi|7710143|ref|NP_002375.1|[7710143]

☐**14:** NP_056669 BLink, Domains, Links
methyl-CpG binding domain protein 1 isoform 3 [Homo sapiens]
gi|7710135|ref|NP_056669.1|[7710135]

☐**15:** NP_004370 BLink, Domains, Links
cAMP responsive element binding protein 1 isoform A; cAMP-response element-binding protein-1; active transcription factor CREB; transactivator protein [Homo sapiens]
gi|4758054|ref|NP_004370.1|[4758054]

☐**16:** BAC48664 BLink, Domains, Links
vanillate O-demethylase oxidoreductase [Bradyrhizobium japonicum USDA 110]
gi|27351658|dbj|BAC48664.1|[27351658]

☐**17:** BAC47655 BLink, Domains, Links
vanillate O-demethylase oxygenase subunit [Bradyrhizobium japonicum USDA 110]
gi|27350645|dbj|BAC47655.1|[27350645]

☐**18:** NP_770039 BLink, Domains, Links
vanillate O-demethylase oxidoreductase [Bradyrhizobium japonicum]
gi|27378510|ref|NP_770039.1|[27378510]

☐**19:** NP_769030 BLink, Domains, Links
vanillate O-demethylase oxygenase subunit [Bradyrhizobium japonicum]
gi|27377501|ref|NP_769030.1|[27377501]

☐ **20:** XP_192834 BLink, Domains, Links

methyl-CpG binding domain protein 2 [Mus musculus]
gi|25054585|ref|XP_192834.1|[25054585]

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Items 1-20 of 42 Page 1 of 3 Next

☐**21:** XP_227444 BLink, Domains, Links
similar to Histone-lysine N-methyltransferase, H3 lysine-9 specific 4 (Histone H3-K9 methyltransferase 4) (H3-K9-HMTase 4) (SET domain bifurcated 1) (ERG-associated protein with SET domain) (ESET) [Rattus norvegicus]
gi|27693569|ref|XP_227444.1|[27693569]

☐**22:** XP_222315 BLink, Domains, Links
similar to Bromodomain adjacent to zinc finger domain 2A (Transcription termination factor-I interacting protein 5) (TTF-I interacting protein 5) (Tip5) [Rattus norvegicus]
gi|27710504|ref|XP_222315.1|[27710504]

☐**23:** XP_215740 BLink, Domains, Links
similar to Bromodomain adjacent to zinc finger domain 2B (hWALp4) [Rattus norvegicus]
gi|27699091|ref|XP_215740.1|[27699091]

Related resources

☐**24:** BAC55657 BLink, Domains, Links
putative cytochrome P450(Obtusifoliol 14-alpha demethylase) [Oryza sativa (japonica cultivar-group)]
gi|27817891|dbj|BAC55657.1|[27817891]

☐**25:** NP_108417 BLink, Domains, Links
probable N-methylproline demethylase (stahydrine utilization protein stcD) [Mesorhizobium loti]
gi|13476848|ref|NP_108417.1|[13476848]

☐**26:** NP_107668 BLink, Domains, Links
vanillate O-demethylase oxidoreductase [Mesorhizobium loti]
gi|13476098|ref|NP_107668.1|[13476098]

☐**27:** NP_498673 BLink, Domains, Links
Methyl-CpG binding domain and DDT domain and PHD-finger and Bromodomain containing protein [Caenorhabditis elegans]
gi|17557087|ref|NP_498673.1|[17557087]

☐**28:** NP_498848 BLink, Domains, Links
DNA topoisomerase II [Caenorhabditis elegans]

gi|17554480|ref|NP_498848.1|[17554480]

☐**29:** A31854 BLink, Domains, Links
lanosterol 14alpha-demethylase (EC 1.14.14.-) cytochrome P450 51 - yeast (Candida tropicalis)
gi|83929|pir||A31854[83929]

☐**30:** A27491 BLink, Domains, Links
lanosterol 14alpha-demethylase (EC 1.14.14.-) cytochrome P450 51 - yeast (Saccharomyces cerevisiae)
gi|82967|pir||A27491[82967]

☐**31:** Q12645 BLink, Domains, Links
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gi|3929362|sp|Q12645|PID9_FUSSO[3929362]

☐**32:** BAC20841 BLink, Domains, Links
putative cytochrome P450(Obtusifoliol 14-alpha demethylase) [Oryza sativa (japonica cultivar-group)]
gi|23617163|dbj|BAC20841.1|[23617163]

☐**33:** BAC20835 BLink, Domains, Links
putative cytochrome P450(Obtusifoliol 14-alpha demethylase) [Oryza sativa (japonica cultivar-group)]
gi|23617157|dbj|BAC20835.1|[23617157]

☐**34:** NP_524468 BLink, Domains, Links
six-banded [Drosophila melanogaster]
gi|17738157|ref|NP_524468.1|[17738157]

☐**35:** AAH32322 BLink, Domains, Links
cytochrome P450, 51 (lanosterol 14-alpha-demethylase) [Homo sapiens]
gi|21619563|gb|AAH32322.1|[21619563]

☐**36:** AAA53284 BLink, Domains, Links
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gi|576547|gb|AAA53284.1|[576547]

☐**37:** CAB58427 BLink, Links
P450 lanosterol 14a demethylase [Cryptococcus neoformans var. neoformans]
gi|6065767|emb|CAB58427.1|[6065767]

☐**38:** BAB53878 BLink, Domains, Links
probable N-methylproline demethylase [Mesorhizobium loti]
gi|14027609|dbj|BAB53878.1|[14027609]

☐**39:** BAB53454 BLink, Domains, Links
vanillate O-demethylase oxidoreductase [Mesorhizobium loti]

gi|14026858|dbj|BAB53454.1|[14026858]

☐ **40:** BAA15607 BLink, Domains, Links

Vanillate demethylase oxidoreductase (EC 1.-.-.-) (Vanillate degradation ferredoxin-like protein). [Escherichia coli]
gi|1736436|dbj|BAA15607.1|[1736436]

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☐ **41:** BAA15598 BLink, Domains, Links

Vanillate demethylase oxidoreductase (EC 1.-.-.-) (Vanillate degradation ferredoxin-like protein). [Escherichia coli]
gi|1736426|dbj|BAA15598.1|[1736426]

☐ **42:** AAA34379 BLink, Domains, Links

14-alpha-demethylase (14DM)
gi|170946|gb|AAA34379.1|[170946]

Related resources

☐ 1: NP_056647. methyl-CpG bindin...[gi:7710145] BLink, Domains, Links

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LOCUS       MBD2                      302 aa            linear   PRI 06-APR-2003
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DBSOURCE    REFSEQ: accession NM_015832.2
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  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 302)
  AUTHORS   Krithivas,A., Fujimuro,M., Weidner,M., Young,D.B. and Hayward,S.D.
  TITLE     Protein interactions targeting the latency-associated nuclear
            antigen of Kaposi's sarcoma-associated herpesvirus to cell
            chromosomes
  JOURNAL   J. Virol. 76 (22), 11596-11604 (2002)
  MEDLINE   22276359
   PUBMED   12388720
  REMARK    GeneRIF: interacts with latency-associated nuclear antigen of
            Kaposi's Sarcoma-associated herpesvirus (KSHV)to tether KSHV to
            cell chromosomes
REFERENCE   2  (residues 1 to 302)
  AUTHORS   Brackertz,M., Boeke,J., Zhang,R. and Renkawitz,R.
  TITLE     Two highly related p66 proteins comprise a new family of potent
            transcriptional repressors interacting with MBD2 and MBD3
  JOURNAL   J. Biol. Chem. 277 (43), 40958-40966 (2002)
  MEDLINE   22287387
   PUBMED   12183469
  REMARK    GeneRIF: interaction with two highly related p66 proteins
REFERENCE   3  (residues 1 to 302)
  AUTHORS   Detich,N., Theberge,J. and Szyf,M.
  TITLE     Promoter-specific activation and demethylation by MBD2/demethylase
  JOURNAL   J. Biol. Chem. 277 (39), 35791-35794 (2002)
  MEDLINE   22229441
   PUBMED   12177048
  REMARK    GeneRIF: MBD2 protein activates CpG sites within the promoter
            region of reporter genes
REFERENCE   4  (residues 1 to 302)
  AUTHORS   Bakker,J., Lin,X. and Nelson,W.G.
  TITLE     Methyl-CpG binding domain protein 2 represses transcription from
            hypermethylated pi-class glutathione S-transferase gene promoters
            in hepatocellular carcinoma cells
  JOURNAL   J. Biol. Chem. 277 (25), 22573-22580 (2002)
  MEDLINE   22063361
   PUBMED   11960994
  REMARK    GeneRIF: Methyl-CpG binding domain protein 2 represses
            transcription from hypermethylated pi-class glutathione
            S-transferase gene promoters in hepatocellular carcinoma cells
REFERENCE   5  (residues 1 to 302)
  AUTHORS   Ng,H.H., Zhang,Y., Hendrich,B., Johnson,C.A., Turner,B.M.,
            Erdjument-Bromage,H., Tempst,P., Reinberg,D. and Bird,A.
```

TITLE MBD2 is a transcriptional repressor belonging to the MeCP1 histone deacetylase complex
JOURNAL Nat. Genet. 23 (1), 58-61 (1999)
MEDLINE 99400553
PUBMED 10471499
REFERENCE 6 (residues 1 to 302)
AUTHORS Hendrich,B., Abbott,C., McQueen,H., Chambers,D., Cross,S. and Bird,A.
TITLE Genomic structure and chromosomal mapping of the murine and human Mbd1, Mbd2, Mbd3, and Mbd4 genes
JOURNAL Mamm. Genome 10 (9), 906-912 (1999)
MEDLINE 99373255
PUBMED 10441743
REFERENCE 7 (residues 1 to 302)
AUTHORS Bhattacharya,S.K., Ramchandani,S., Cervoni,N. and Szyf,M.
TITLE A mammalian protein with specific demethylase activity for mCpG DNA
JOURNAL Nature 397 (6720), 579-583 (1999)
MEDLINE 99158138
PUBMED 10050851
REFERENCE 8 (residues 1 to 302)
AUTHORS Hendrich,B. and Bird,A.
TITLE Identification and characterization of a family of mammalian methyl-CpG binding proteins
JOURNAL Mol. Cell. Biol. 18 (11), 6538-6547 (1998)
MEDLINE 98449942
PUBMED 9774669
REFERENCE 9 (residues 1 to 302)
AUTHORS Scanlan,M.J., Chen,Y.T., Williamson,B., Gure,A.O., Stockert,E., Gordan,J.D., Tureci,O., Sahin,U., Pfreundschuh,M. and Old,L.J.
TITLE Characterization of human colon cancer antigens recognized by autologous antibodies
JOURNAL Int. J. Cancer 76 (5), 652-658 (1998)
MEDLINE 98272252
PUBMED 9610721
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from AF120989.1, AF120989.1 and AF120994.1.

Summary: DNA methylation is the major modification of eukaryotic genomes and plays an essential role in mammalian development. Human proteins MECP2, MBD1, MBD2, MBD3, and MBD4 comprise a family of nuclear proteins related by the presence in each of a methyl-CpG binding domain (MBD). Each of these proteins, with the exception of MBD3, is capable of binding specifically to methylated DNA. MECP2, MBD1 and MBD2 can also repress transcription from methylated gene promoters. MBD2 may function as mediators of the biological consequences of the methylation signal. It is also reported that the MBD2 protein functions as a demethylase to activate transcription, as DNA methylation causes gene silencing. However, MBD2 in HeLa cells does not demethylate DNA, probably due to HeLa cell's using an alternative pathway involving MBD2 to silence methylated genes.

Transcript Variant: This variant (testis-specific) includes an alternate exon located within intron 2 resulting in a distinct COOH terminus.

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☐1: NP_056647. methyl-CpG bindin...[gi:7710145] BLink, Domains, Links

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DEFINITION  methyl-CpG binding domain protein 2 testis-specific isoform [Homo
            sapiens].
ACCESSION   NP_056647
VERSION     NP_056647.1  GI:7710145
DBSOURCE    REFSEQ: accession NM_015832.2
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SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 302)
  AUTHORS   Krithivas,A., Fujimuro,M., Weidner,M., Young,D.B. and Hayward,S.D.
  TITLE     Protein interactions targeting the latency-associated nuclear
            antigen of Kaposi's sarcoma-associated herpesvirus to cell
            chromosomes
  JOURNAL   J. Virol. 76 (22), 11596-11604 (2002)
  MEDLINE   22276359
   PUBMED   12388720
  REMARK    GeneRIF: interacts with latency-associated nuclear antigen of
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REFERENCE   2  (residues 1 to 302)
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  MEDLINE   22287387
   PUBMED   12183469
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  TITLE     Promoter-specific activation and demethylation by MBD2/demethylase
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  MEDLINE   22229441
   PUBMED   12177048
  REMARK    GeneRIF: MBD2 protein activates CpG sites within the promoter
            region of reporter genes
REFERENCE   4  (residues 1 to 302)
  AUTHORS   Bakker,J., Lin,X. and Nelson,W.G.
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   PUBMED   11960994
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            S-transferase gene promoters in hepatocellular carcinoma cells
REFERENCE   5  (residues 1 to 302)
  AUTHORS   Ng,H.H., Zhang,Y., Hendrich,B., Johnson,C.A., Turner,B.M.,
            Erdjument-Bromage,H., Tempst,P., Reinberg,D. and Bird,A.
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TITLE MBD2 is a transcriptional repressor belonging to the MeCP1 histone deacetylase complex
JOURNAL Nat. Genet. 23 (1), 58-61 (1999)
MEDLINE 99400553
PUBMED 10471499
REFERENCE 6 (residues 1 to 302)
AUTHORS Hendrich,B., Abbott,C., McQueen,H., Chambers,D., Cross,S. and Bird,A.
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JOURNAL Mamm. Genome 10 (9), 906-912 (1999)
MEDLINE 99373255
PUBMED 10441743
REFERENCE 7 (residues 1 to 302)
AUTHORS Bhattacharya,S.K., Ramchandani,S., Cervoni,N. and Szyf,M.
TITLE A mammalian protein with specific demethylase activity for mCpG DNA
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JOURNAL Mol. Cell. Biol. 18 (11), 6538-6547 (1998)
MEDLINE 98449942
PUBMED 9774669
REFERENCE 9 (residues 1 to 302)
AUTHORS Scanlan,M.J., Chen,Y.T., Williamson,B., Gure,A.O., Stockert,E., Gordan,J.D., Tureci,O., Sahin,U., Pfreundschuh,M. and Old,L.J.
TITLE Characterization of human colon cancer antigens recognized by autologous antibodies
JOURNAL Int. J. Cancer 76 (5), 652-658 (1998)
MEDLINE 98272252
PUBMED 9610721
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from AF120989.1, AF120989.1 and AF120994.1.

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//
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1: Nature 1999 Feb 18;397(6720):568-9

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